

**IN THE CLAIMS**

Kindly cancel claims 1-99 and substitute the following claims therefore:

--100. (New) A method of screening for a compound that modulates, inhibits or activates sweet taste signaling comprising:

(i) contacting a cell that co-expresses T1R2 and T1R3 polypeptides to produce a hetero-oligomeric taste receptor that responds to sweet stimuli with a putative sweet taste modulatory compound; and

(ii) assaying the effect of said putative sweet taste modulatory compound on the activity of said hetero-oligomeric taste receptor and determining whether said compound modulates, inhibits or activates sweet taste signaling based on said activity assay.

101. (New) A method of screening for a compound that modulates, enhances or inhibits activation of the T1R2/T1R3 sweet receptor by a known sweet compound comprising:

(i) contacting a cell that co-expresses T1R2 and T1R3 polypeptides to produce a hetero-oligomeric taste receptor that responds to sweet stimuli with a putative sweet taste modulatory compound and with a known sweet compound; and

(ii) measuring the effect of said putative sweet taste modulatory compound on the activation of said hetero-oligomeric taste receptor by said known sweet compound.

102. (New) The method of claim 100 wherein said cell is a eukaryotic cell.

103. (New) The method of claim 101 wherein said cell is a eukaryotic cell.

104. (New) The method of claim 102 wherein said eukaryotic cell is a mammalian cell.

105. (New) The method of claim 103 wherein said eukaryotic cell is a mammalian cell.

106. (New) The method of claim 104 wherein said mammalian cell is a CHO, Hela or HEK-293 cell.

107. (New) The method of claim 105 wherein said mammalian cell is a CHO, Hela or HEK-293 cell.

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108. (New) The method of claim 100 wherein said cell expresses a G protein that couples said T1R polypeptides.

109. (New) The method of claim 101 wherein said cell expresses a G protein that couples said T1R polypeptides.

110. (New) The method of claim 108 wherein said G protein is  $G_{\alpha 15}$  or  $G_{\alpha 16}$ .

110a. (New) The method of claim 109 wherein said G protein is  $G_{\alpha 15}$  or  $G_{\alpha 16}$ .

111. (New) The method of claim 100 wherein the activity of said taste receptor is measured by detecting changes in intracellular  $Ca^{2+}$  levels.

112. (New) The method of claim 101 wherein the activity of said taste receptor is measured by detecting changes in intracellular  $Ca^{2+}$  levels.

113. (New) The method of claim 111 wherein said  $Ca^{2+}$  levels are detected using an ion sensitive or membrane voltage fluorescent indicator.

114. (New) The method of claim 112 wherein said  $Ca^{2+}$  levels are detected using an ion sensitive or membrane voltage fluorescent indicator.

115. (New) The method of claim 100 wherein taste receptor activity is detected by monitoring changes in ionic polarization.

116. (New) The method of claim 101 wherein taste receptor activity is detected by monitoring changes in ion polarization.

117. (New) The method of claim 100, wherein taste receptor activity is measured by detecting changes in second messenger levels.

118. (New) The method of claim 101, wherein taste receptor activity is measured by detecting changes in second messenger levels.

119. (New) The method of claim 117, wherein said second messenger is IP3.

120. (New) The method of claim 118, wherein said second messenger is IP3.

121. (New) The method of claim 100, wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.

122. (New) The method of claim 101, wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.

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123. (New) The method of claim 121, wherein said cyclic nucleotide is cAMP or cGMP.

124. (New) The method of claim 122, wherein said cyclic nucleotide is cAMP or cGMP.

125. (New) The method of claim 100, wherein taste receptor activity is detected by measuring changes in  $\text{Ca}^{2+}$  levels by fluorimetric imaging.

126. (New) The method of claim 101, wherein taste receptor activity is detected by measuring changes in  $\text{Ca}^{2+}$  levels by fluorimetric imaging.

127. (New) The method of claim 111, wherein changes in taste receptor activity are detected by measuring changes in FURA-2, FURA-3, or Fluo-4 dependent fluorescence in the cell.

128. (New) The method of claim 112, wherein changes in receptor activity are detected by measuring changes in FURA-2, FURA-3, or Fluo-4 dependent fluorescence in the cell.

129. (New) The method of claim 100, wherein changes in taste receptor activity are detected by measuring changes in G protein binding of  $\text{GTP}\gamma\text{S}$ .

130. (New) The method of claim 101, wherein changes in taste receptor activity are detected by measuring changes in G protein binding of  $\text{GTP}\gamma\text{S}$ .

131. (New) The method of claim 100, wherein changes in the activity of said taste receptor are detected by an assay that monitors a ligand in the kinase/arrestin pathway.

132. (New) The method of claim 101, wherein changes in the activity of said taste receptor are detected by an assay that monitors a ligand in the kinase/arrestin pathway.

133. (New) The method of claim 100, which is a high throughput screening assay.

134. (New) The method of claim 101, which is a high throughput screening assay.

135. (New) The method of claim 133, wherein said assay includes the use of a combinatorial chemical library.

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136. (New) The method of claim 134, wherein said assay includes the use of a combinatorial chemical library.

137. (New) The method of claim 100, wherein said T1R2 and T1R3 polypeptides are human, rat or mouse T1R2 and T1R3 polypeptides.

138. (New) The method of claim 101, wherein said T1R2 and T1R3 polypeptides are human, rat or mouse T1R2 and T1R3 polypeptides.

139. (New) The method of claim 100, wherein said T1R2 and T1R3 polypeptides are human T1R2 and human T1R3 polypeptides.

140. (New) The method of claim 101, wherein said T1R2 and T1R3 polypeptides are human T1R2 and human T1R3 polypeptides.

141. (New) The method of claim 101, wherein said known sweet ligand is selected from the group activity of cyclamate, sucrose, fructose, neotame, aspartame, saccharin and AcesulfameK.

142. (New) The method of claim 100, wherein said putative taste modulatory compound enhances the activity of said taste receptor.

143. (New) The method of claim 101, wherein said putative taste modulatory compound enhances the activation of said taste receptor by said known sweet compound.

144. (New) The method of claim 100, wherein said putative taste modulatory compound inhibits the activity of said taste receptor.

145. (New) The method of claim 101, wherein said putative taste modulatory compound inhibits activation of said taste receptor by said known sweet compound.

146. (New) The method of claim 100, wherein said T1R2 and T1R3 polypeptides are encoded by the DNA sequences contained in SEQ ID NO: 3 and SEQ ID NO: 5 respectively or a DNA that specifically hybridizes respectively to each of said DNA under moderately stringent hybridization conditions and co-expression thereof results in a taste receptor that responds to sweet taste stimuli.

146. (New) The method of claim 101, wherein said T1R2 and T1R3 polypeptides are encoded by the DNA sequences contained in SEQ ID NO: 3 and SEQ ID NO: 5 respectively or a DNA that specifically hybridizes respectively to each of said

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5/3/03 <sup>a3</sup> DNA under moderately stringent hybridization conditions and co-expression thereof  
results in a taste receptor that responds to sweet taste stimuli.